Supplemental materials

Table S1: Alternative options for anti-*Toxoplasma* SAR-based optimization studies

Anti-*Toxoplasma* TS-4					
[a]Compound	*MW	*AlogP	[b]IC_{50} *T. gondii* (µM)	[c]CC_{50} HFF (µM)	[d]SI
MMV007273	480.57746	7.242	5.85	>30	>5.12
MMV666597	451.55946	8.149	6.28	>30	>4.78
MMV665820	293.53048	3.134	6.45	>30	>4.65
MMV006937	279.33638	4.353	8.22	>30	>3.65
MMV007591	496.68135	4.959	8.23	>30	>3.64
MMV009063	322.44394	4.479	8.72	>30	>3.44
MMV665886	385.86393	4.956	10.46	>30	>2.87
MMV085471	465.60917	7.814	11.16	>30	>2.69
MMV000483	341.44397	4.449	12.85	>30	>2.33
MMV665888	440.4474	4.475	13.15	>30	>2.28
MMV666023	453.53712	8.504	13.48	>30	>2.23
MMV019266	312.41258	4.458	13.93	>30	>2.15
MMV665809	395.72119	4.615	14.46	>30	>2.07
MMV666124	403.90566	3.902	14.92	>30	>2.01
MMV000444	367.48456	4.551	17.89	>30	>1.67
MMV001049	269.38132	3.634	18.07	>30	>1.66
MMV006389	359.41606	5.251	18.66	>30	>1.60
MMV666057	420.67648	4.242	19.04	>30	>1.57
MMV000442	315.83708	5.336	20.4	>30	>1.47
MMV667487	260.3381	1.121	20.6	>30	>1.45
MMV006429	409.50132	3.582	20.85	>30	>1.43
MMV019066	359.39958	1.599	20.93	>30	>1.43
MMV018984	278.30526	3.271	21.06	>30	>1.42
MMV665789	261.74664	3.751	21.37	>30	>1.40
MMV007571	301.40326	3.619	22.3	>30	>1.34
MMV666108	400.94155	3.86	24.04	>30	>1.24
MMV665971	484.95193	4.858	24.93	>30	>1.20
MMV019758	405.48947	4.252	25.68	>30	>1.19
MMV000448	279.37944	3.363	25.84	>30	>1.16
MMV008270	265.3098	3.867	26.2	>30	>1.14
MMV665953	333.57282	4.721	26.49	>30	>1.13
MMV019662	465.58449	4.632	26.62	>30	>1.12
MMV396744	405.46796	4.309	26.75	>30	>1.12
MMV665850	273.71758	3.229	26.83	>30	>1.10
MMV666110	411.62324	4.233	27.05	>30	>1.10
MMV019199	266.29786	2.598	28.12	>30	>1.06
MMV007695	657.7524	7.237	28.92	>30	>1.03
MMV080034	254.26234	2.82	28.99	>30	>1.03
PYR	-	-	3.62	-	-

SDZ	-	-	26.05	-	-

[a]Compounds are designated by their MMV identifier codes; [b]Compounds were serially diluted and tested in culture. Results are means from triplicate experiments; [c]Cell cytotoxicity was evaluated in culture against Human Foreskin Fibroblasts and results expressed as means of triplicate experiments; [d]Selectivity indices were calculated based on the ratio CC_{50}(HFF)/IC_{50} Test drugs; [*]Molecular weights and AlogP values were gotten as supporting information to the Malaria Box. Positive controls (PYR: Pyrimethamine; SDZ: Sulfadiazine; MTZ: Metronidazole).

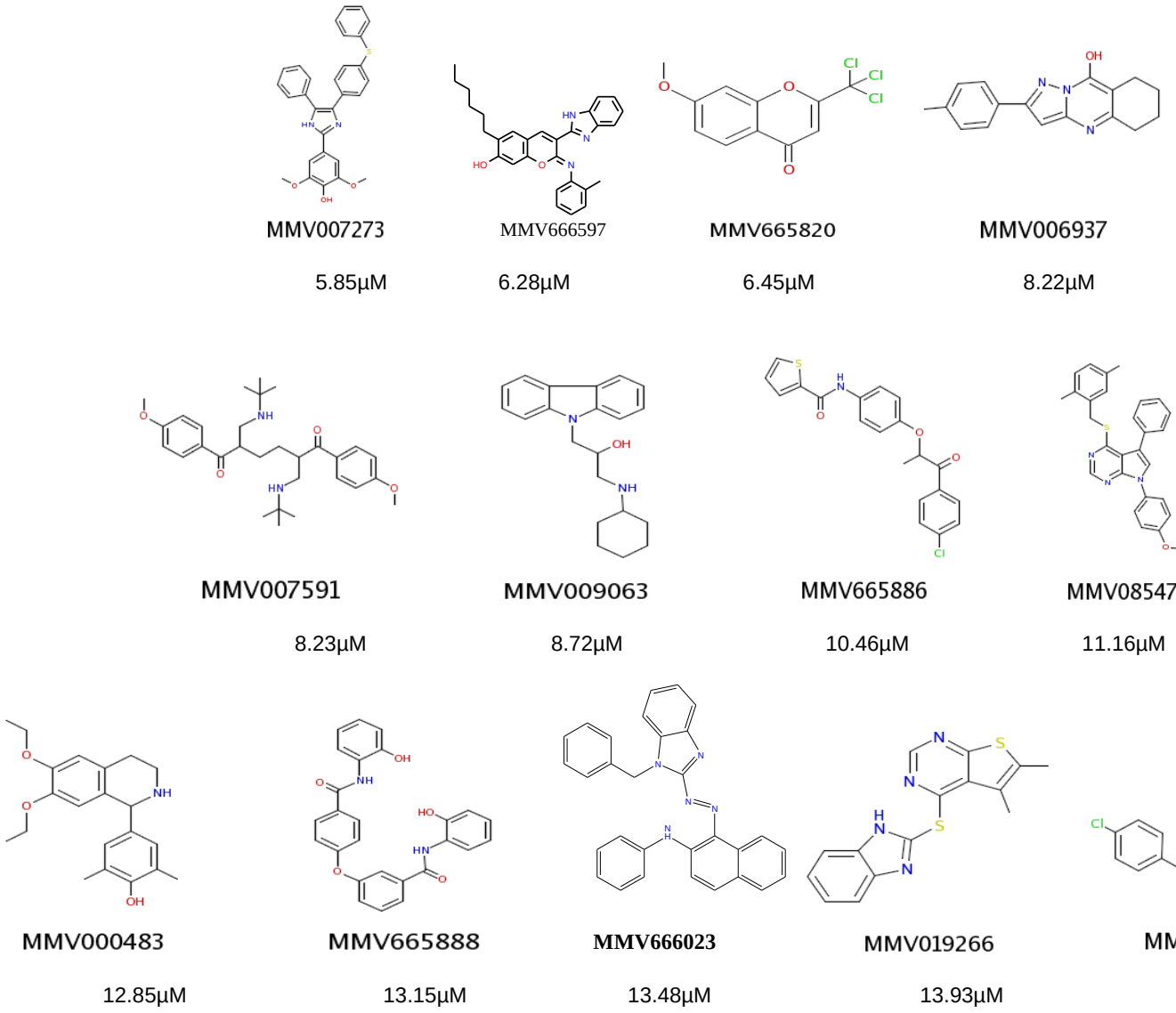
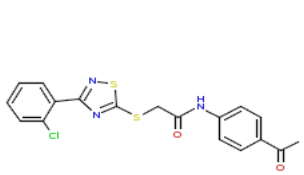
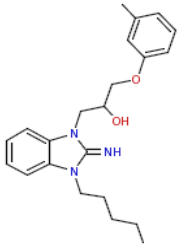


Fig. S2: Structures and activity of MMV Malaria Box compounds against *T. gondii* TS-4 *in vitro*



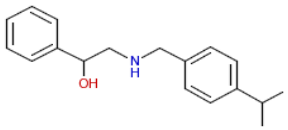
MMV666124

14.92µM



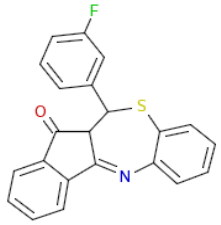
MMV000444

17.89µM



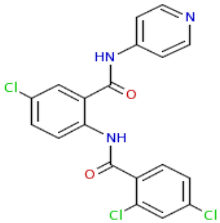
MMV001049

18.07µM



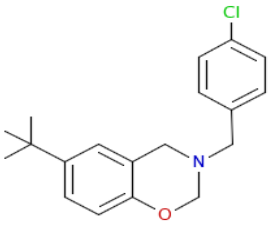
MMV006389

18.66µM



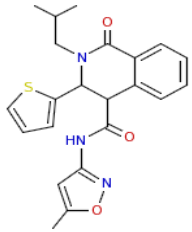
MMV666057

19.04µM



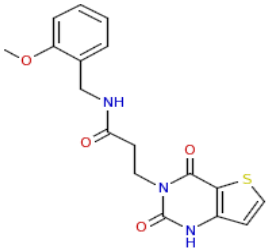
MMV000442

20.40µM



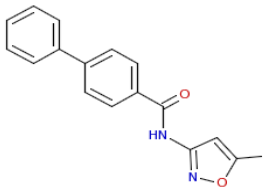
MMV006429

20.85µM



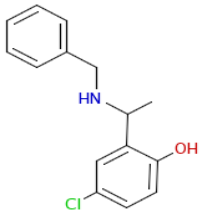
MMV019066

20.93µM



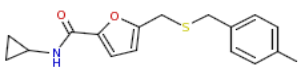
MMV018984

21.06µM



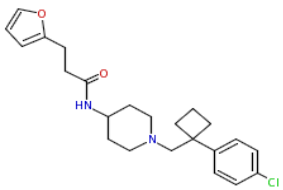
MMV665789

21.37µM



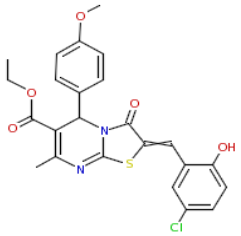
MMV007571

22.30µM



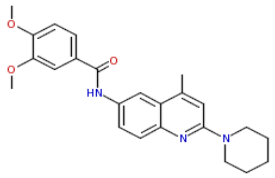
MMV666108

24.04µM



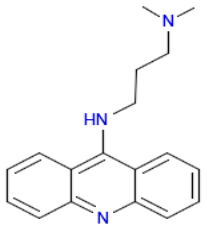
MMV665971

24.93µM



MMV019758

25.68µM



MMV000448

25.84µM

Fig. S2 cont'd (1): Structures and activity of MMV Malaria Box compounds against *T. gondii* TS-4 *in vitro*

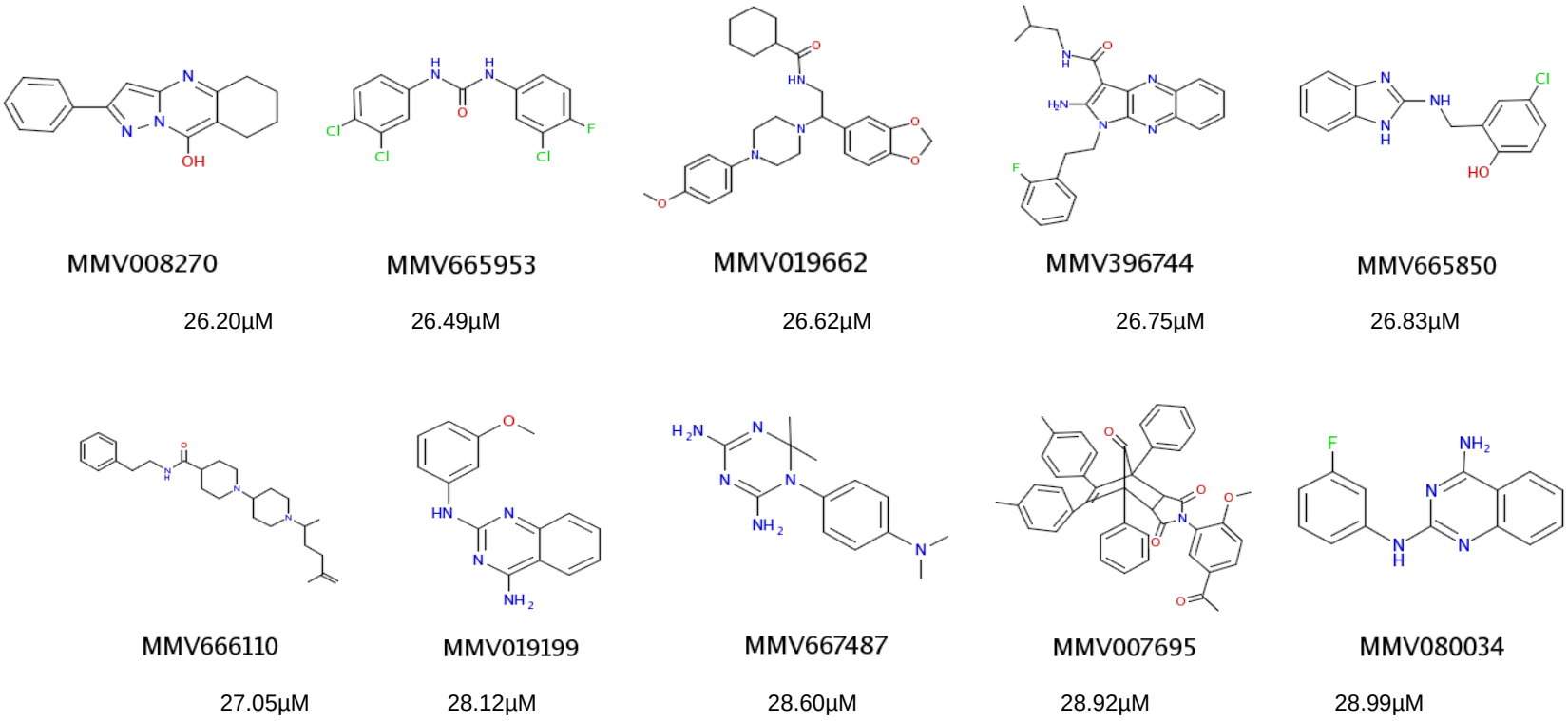


Fig. S2 cont'd (2): Structures and activity of MMV Malaria Box compounds against *T. gondii* TS-4 *in vitro.*

MMV identifiers and structures were provided by the MMV as part of the supporting information for the Open Access Malaria Box. Triplicate concentrations of serially diluted compounds were tested *in vitro* against *Toxoplasma gondii* TS-4 strain tachyzoites. IC_{50} (50% inhibitory concentration) values were calculated from sigmoidal dose-response curves. Structure, MMV identifier, and IC_{50} are shown for each listed compound.

S3: Sigmoidal Dose-Response Analysis Data

Malaria Box compounds hit *Toxoplasma* and *Entamoeba*

Anti-*Toxoplasma activity*

MMV007791

log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	-0.7265
HillSlope	0.3372
IC50	0.1877
Std. Error	
LogIC50	0.08953
HillSlope	0.03020
95% Confidence Intervals	
LogIC50	-0.9163 to -0.5367
HillSlope	0.2732 to 0.4012
IC50	0.1213 to 0.2906
Goodness of Fit	
Degrees of Freedom	16
R square	0.9111
Absolute Sum of Squares	297.5
Sy.x	4.312
Number of points Analyzed	18

MMV006704

log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.2890
HillSlope	0.7658
IC50	**1.945**
Std. Error	
LogIC50	0.09433
HillSlope	0.1435
95% Confidence Intervals	
LogIC50	0.07144 to 0.5065
HillSlope	0.4349 to 1.097
IC50	1.179 to 3.210
Goodness of Fit	
Degrees of Freedom	8
R square	**0.8411**
Absolute Sum of Squares	406.4
Sy.x	7.127
Number of points Analyzed	10

MMV007881

log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.02895
HillSlope	0.4256
IC50	**1.069**
Std. Error	
LogIC50	0.1556
HillSlope	0.08035
95% Confidence Intervals	
LogIC50	-0.3299 to 0.3878
HillSlope	0.2403 to 0.6109
IC50	0.4679 to 2.442
Goodness of Fit	
Degrees of Freedom	8
R square	**0.7933**
Absolute Sum of Squares	194.1
Sy.x	4.925
Number of points Analyzed	10

MMV007363

log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.1736
HillSlope	0.2945
IC50	**1.491**
Std. Error	
LogIC50	0.1814
HillSlope	0.06941
95% Confidence Intervals	
LogIC50	-0.2447 to 0.5918
HillSlope	0.1345 to 0.4546
IC50	0.5692 to 3.907
Goodness of Fit	
Degrees of Freedom	8
R square	**0.7047**
Absolute Sum of Squares	193.2
Sy.x	4.914
Number of points Analyzed	10

MMV020548

log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.5854
HillSlope	0.7808
IC50	3.850
Std. Error	

LogIC50	0.06816
HillSlope	0.1300
95% Confidence Intervals	
LogIC50	“0.4283 to 0.7426”
HillSlope	“0.4812 to 1.081”
IC50	“2.681 to 5.529”
Goodness of Fit	
Degrees of Freedom	8
R square	**0.8590**
Absolute Sum of Squares	456.4
Sy.x	7.554
Number of points Analyzed	10

	MMV085203
log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.6571
HillSlope	0.7855
IC50	**4.541**
Std. Error	
LogIC50	0.08279
HillSlope	0.1636
95% Confidence Intervals	
LogIC50	“0.4662 to 0.8480”
HillSlope	“0.4082 to 1.163”
IC50	“2.926 to 7.048”
Goodness of Fit	
Degrees of Freedom	8
R square	**0.8006**
Absolute Sum of Squares	755.9
Sy.x	9.720
Number of points Analyzed	10

	MMV666095
log(inhibitor) vs. normalized response – Variable slope	
Best-fit values	
LogIC50	0.4840
HillSlope	1.046
IC50	**3.048**
Std. Error	
LogIC50	0.07736
HillSlope	0.2242
95% Confidence Intervals	
LogIC50	“0.3056 to 0.6624”
HillSlope	“0.5292 to 1.563”

IC50	“2.021 to 4.596”
Goodness of Fit	
Degrees of Freedom	8
R square	**0.8340**
Absolute Sum of Squares	817.5
Sy.x	10.11
Number of points	
Analyzed	10

Anti-*Entamoeba activity*

	MMV666600
log(inhibitor) vs. response -- Variable slope (four parameters)	
Best-fit values	
Bottom	41.05
Top	99.85
LogIC50	1.028
HillSlope	4.543
IC50	**10.66**
Span	58.80
Std. Error	
Bottom	3.063
Top	4.584
LogIC50	0.04604
HillSlope	1.263
Span	5.690
95% Confidence Intervals	
Bottom	33.56 to 48.54
Top	88.63 to 111.1
LogIC50	0.9151 to 1.140
HillSlope	1.454 to 7.633
IC50	8.224 to 13.82
Span	44.87 to 72.72
Goodness of Fit	
Degrees of Freedom	6
R square	**0.9688**
Absolute Sum of Squares	199.9
Sy.x	5.771
Number of points	
Analyzed	10

	MMV006861
log(agonist) vs. response -- Variable slope (four parameters)	
Best-fit values	
Bottom	19.80
Top	96.06
LogEC50	1.192

HillSlope	5.806
EC50	**15.58**
Span	76.26
Std. Error	
Bottom	2.831
Top	9.028
LogEC50	0.03540
HillSlope	6.667
Span	10.74
95% Confidence Intervals	
Bottom	12.87 to 26.73
Top	73.97 to 118.1
LogEC50	1.106 to 1.279
HillSlope	-10.51 to 22.12
EC50	12.76 to 19.01
Span	49.98 to 102.5
Goodness of Fit	
Degrees of Freedom	6
R square	**0.9790**
Absolute Sum of Squares	185.2
Sy.x	5.556
Number of points Analyzed	10